REMARKS

Claims 1-20 have been canceled without prejudice or disclaimer. Claims 69 and 70 have been added and therefore are pending in the present application. Claims 69 and 70 are supported by claims 1-68. The phrase "competitive IgE ELISA assay" is supported by page 56, lines 27-32 of the specification.

The specification has been amended to correct inadvertent typographical errors.

It is respectfully submitted that the present amendment presents no new issues or new matter and places this case in condition for allowance. Reconsideration of the application in view of the above amendments and the following remarks is requested.

I. The Rejection of Claims 1-20 under 35 U.S.C. 112

Claims 1-20 are rejected under 35 U.S.C. 112 "because the specification, while being enabling for enzyme[s], does not reasonably provide enablement for the broadly claimed method using a library of protein variants." This rejection is respectfully traversed.

The present invention relates to methods for selecting a variant of a protein with reduced immunogenicity. The specification contains examples demonstrating the use of Applicants' claimed method in selecting variants of enzymes. Based on Applicants' disclosure, one of ordinary skill in the art would expect that Applicants' claimed methods could be applied to any protein.

For the foregoing reasons, Applicants submit that the claims overcome this rejection under 35 U.S.C. 112. Applicants respectfully request reconsideration and withdrawal of the rejection.

II. The Rejection of Claims 1-20 under 35 U.S.C. 112

Claims 1-20 are rejected under 35 U.S.C. 112 as being indefinite. Claims 1-20 have been rewritten as claims 69 and 70 to address this rejection. Applicants therefore submit that this rejection has been overcome.

III. The Rejections of Claims 1-20 under the Doctrine of Obviousness-Type Double Patenting

Claims 1-20 are rejected under the doctrine of obviousness-type double patenting as being unpatentable over claims 55-73 of application nos. 09/417,608 and 09/695,173. This rejection is respectfully traversed.

Applicants submit that this rejection is premature. The 608 and 173 applications have not yet been allowed. Once th y hav been allowed, Applicants will consider filing a terminal disclaimer.

IV. The Rejection of Claims 1-5, 8-10 and 12-20 under 35 U.S.C. 102

Claims 1-5, 8-10 and 12-20 are rejected under 35 U.S.C. 102(a) as being anticipated by Sosin et al. (WO 99/38978). This rejection is respectfully traversed.

Sosin et al. disclose a method for preparing modified allergens that are less reactive with IgE. The method includes identifying IgE binding sites on allergens, modifying said binding sites by mutation or blocking the binding sites, screening the modified allergens for binding to IgE and selecting modified allergens having a decrease binding to IgE (claim 1). In the examples, Sosin et al. synthesize peptides corresponding to epitopes of peanut storage proteins Ara h1, Ara h2 and Ara h3 and mutants thereof (i.e., fragments and not the entire protein), which are tested for IgE (and IgG) binding capabilities.

However, Sosin et al. do not disclose a method comprising generating a diversified DNA library of genes encoding variants of the protein. Moreover, Sosin et al. do not disclose a method comprising the use of competitive ELISA to identify variants with reduced immunogenicity.

For the foregoing reasons, Applicants submit that the claims overcome this rejection under 35 U.S.C. 102. Applicants respectfully request reconsideration and withdrawal of the rejection.

V. The Rejection of Claims 1-5, 8-10 and 12-20 under 35 U.S.C. 102

Claims 1-5, 8-10 and 12-20 are rejected under 35 U.S.C. 102(b) as being anticipated by Jespers et al. (J. Mol. Biol., 269: 704-718 (1997)), Williams et al. (J. Immunological Methods, 213: 1-17 (1998)) or Collen et al. (WO 96/21016). This rejection is respectfully traversed.

Jespers et al. disclose a method of epitope mapping, comprising preparing a randomiz d library of staphylokinase mutants by error-prone PCR, phage display, and negative selection on binding to antibodies.

William et al. disclose a method for identifying linear epitopes of beta lactoglobulin (BLG) using PEPSCAN and phage display. Specifically, Williams et al. raise an antibody against BLG and subject a library of randomized short peptides to the antibody. Williams et al. then align BLG and the nanopeptides that bind to the antibody.

Collen et al. disclose the production of staphylokinase derivativ s by preparing a DNA fragment coding for an active staphylokinase, performing site-directed mutagenesis on the

fragment to replace one or more codons in the fragment, transforming into a host cell, and cultivating the host cell to express staphylokinas derivative.

However, neither of these references discloses a method comprising the use of competitive ELISA to identify variants with reduced immunogenicity.

For the foregoing reasons, Applicants submit that the claims overcome this rejection under 35 U.S.C. 102. Applicants respectfully request reconsideration and withdrawal of the rejection.

VI. The Rejection of Claims 1-20 under 35 U.S.C. 103

Claims 1-20 are rejected under 35 U.S.C. 103 as being unpatentable over any of Sosin et al., Jespers et al., Williams et al., or Collen et al. in view of Hewinson et al. (WO 97/08322) and applicants' disclosure of known glycosylation sites. This rejection is respectfully traversed.

The Sosin et al., Jespers et al., Williams et al., and Collen et al. references are discussed above in sections IV and V. As explained in these sections, neither of these references teaches or suggests a method comprising the use of competitive ELISA to identify variants with reduced immunogenicity.

Hewinson et al. merely disclose that a post-translational modification such as glycosylation can be used to provide proteins with a glycosylating structure that assists in the secretion from host cells.

However, Hewinson et al. also do not teach or suggest a method comprising the use of competitive ELISA to identify variants with reduced immunogenicity.

For the foregoing reasons, Applicants submit that the claims overcome this rejection under 35 U.S.C. 103. Applicants respectfully request reconsideration and withdrawal of the rejection.

VII. Conclusion

In view of the above, it is respectfully submitted that all claims are in condition for allowance. Early action to that end is respectfully requested. The Examiner is hereby invited to contact the undersigned by telephone if there are any questions concerning this amendment or application.

Respectfully submitted,

Date: March 10, 2003

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Attorn y Dock t No.: 6067.200-US PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Roggen et al Confirmation No: 2466

Serial No.: 09/733,485 Group Art Unit: 1627

Filed: December 8, 2000 Examiner: T. Wessendorf

For: High Throughput Screening (HTS) Assays

VERSION WITH MARKINGS TO SHOW CHANGES MADE

Sir:

Below is a marked-up version of the amendments made in the accompanying amendment.

IN THE SPECIFICATION:

The paragraph on page 45, lines 12-13 has been amended as follows:

A preferred embodiment relates to a method, wherein the spatial array ~~of~~ is of a microtiter plate, a solid surface or a textile surface.

The paragraph on page 60, lines 22-26 has been amended as follows:

Protease libraries producing epitopee variants were established. These variants might or might not be His-tagged. Screening is directly on bacterial culture media, using covalink plates coated with mouse anti-rat IgE monoclonal antibodies saturated with anti-savinase specific rat IgE. The amounts of bound wild type antigen ~~was~~ were determined with a anti-wild type polyclonal rabbit antiserum.

The paragraph on page 61, lines 11-15 has been amended as follows:

50 microliter HRP-labelled species-specific anti-Ig antibody is added and incubated 30 min, then the wells are wash three times in PBS-tween. Finally, 50 microliter ODP-H2O2-mixture is added and A492 is measured kinetically to determine the level of bound antibodi s. Dilutions are adjusted such that th 'backbone protein' gives none or very littl level of bound antibody.